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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 09/993,647
Filing Date: November 27, 2001
Appellant(s): RIEDL ET AL.

Richard J. Traverso

For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed September 3, 2004.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

The amendment after final rejection filed on September 3, 2004 has been entered.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

The appellant's statement of the issues in the brief is correct.

The rejection under 35 U.S.C. 112, second paragraph is hereby withdrawn in view of the amendment to claim 68.

Regarding the provisional obviousness-type double patenting rejection over claims 68-98 of copending application 10/042,203, it was indicated in the Interview Summary (May 6, 2004) that "if the ODP is the only rejection left and the other application is not issued, the rejection will be reconsidered favorably".

(7) Grouping of Claims

Appellant's brief includes a statement that claims 68, 74, 80, 81, 87 and 93 do not stand or fall together and provides reasons as set forth in 37 CFR 1.192(c)(7) and (c)(8).

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

Note: Appendix B correctly lists the appealed claims, however, does not contain a complete listing of all of the claims in the application, including those that have been previously cancelled. Accordingly, a complete listing of all claims is correctly written in the Appendix to the Examiner's Answer.

(9) Prior Art of Record

WO 99/32463	Miller	7-1999

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

1. Claims 74, 80, 81, 87 and 93 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of carcinoma of colon, does not reasonably provide enablement for all other diseases mediated by RAF kinase. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant claims are drawn to the treatment of 'disease mediated by RAF kinase' and according to the specification, the compounds are useful in the treatment of tumors and/or cancerous cell growth mediated by RAF kinase, see specification page 2, lines 5-17. Further, the specification discloses several types of cancers, e.g., solid cancers, myeloid disorders, adenomas. First, the instant claims cover 'diseases' that are known to exist and those that may be discovered in the future, for which there is no enablement provided. Further, no compound has ever been found to treat cancers of all types generally. Since this assertion is contrary to what is known in medicine, proof must be provided that this revolutionary assertion has merits. The existence of such a "silver bullet" is contrary to our present understanding of oncology. Cecil Textbook of Medicine states that "each specific type has unique biologic and clinical features that must be appreciated for proper diagnosis, treatment and study" (see the enclosed article, page 1004). Different types of cancers affect different organs and have different methods of growth and harm to the body. Also see *In re Buting*, 163 USPQ 689 (CCPA 1969), wherein 'evidence involving a single compound and two types of cancer, was held insufficient to establish the utility of the

claims directed to disparate types of cancers'. Thus, it is beyond the skill of oncologists today to get an agent to be effective against cancers and/or diseases mediated by RAF kinase in general.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

1) The nature of the invention: Therapeutic use of the compounds in treating several types of cancers, which include solid cancers, myeloid disorders, adenomas, etc.

2) The state of the prior art: There are no known compounds of similar structure, which have been demonstrated to treat all types of cancers.

3) The predictability or lack thereof in the art: Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use of the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

4) The amount of direction or guidance present and 5) the presence or absence of working examples: There are no doses present to direct one to protect a potential host from the disorders embraced by the instant claims nor there are doses given for the treatment of the disorders recited. The specification provides assays (see pages 94-96) to test the compounds *in vitro* and discloses that the compounds exhibit RAF kinase inhibitory properties. However, there is no

demonstrated correlation that the tests and results apply to all of the disorders embraced by the instant claims.

6) The breadth of the claims: The instant claims embrace the treatment of all diseases mediated by RAF kinase. See *In re Vaeck*, 947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991).

7) The quantity of experimentation needed would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan, regarding the pharmaceutical use, for the reasons stated above.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the use of the invention. In view of the breadth of the claim, the chemical nature of the invention, the unpredictability of ligand-receptor interactions in general, and the lack of working examples regarding the activity of the claimed compounds, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the invention commensurate in scope with the claims.

2. Claims 68, 74, 80, 81, 87 and 93 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miller et al., WO 99/32463. The reference teaches a generic group of compounds which embraces applicant's instantly claimed compounds. See formula I in page 7 and corresponding species in pages 15-16 drawn to 5-tert-butyl-2-methoxyphenyl ureas and 5-trifluoromethyl-2-methoxy-phenyl ureas. The compounds are taught to be useful as pharmaceutical therapeutic agents for the treatment of diseases including cancer, see page 6-7. The claims differ from the reference by reciting a specific species and/or a more limited genus

than the reference. However, it would have been obvious to one having ordinary skill in the art at the time of the invention to select any of the species of the genus taught by the reference, including those instantly claimed, because the skilled chemist would have the reasonable expectation that any of the species of the genus would have similar properties and, thus, the same use as taught for the genus as a whole i.e., as pharmaceutical therapeutic agents. One of ordinary skill in the art would have been motivated to select the claimed compounds from the genus in the reference since such compounds would have been suggested by the reference as a whole. It has been held that a prior art disclosed genus of useful compounds is sufficient to render prima facie obvious a species falling within a genus. *In re Susi*, 440 F.2d 442, 169 USPQ 423, 425 (CCPA 1971), followed by the Federal Circuit in *Merck & Co. v. Biocraft Laboratories*, 847 F.2d 804, 10 USPQ 2d 1843, 1846 (Fed. Cir. 1989).

3. Claims 68, 74, 80, 81, 87 and 93 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-67 (or currently pending) of copending Application No. 10/042,203. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instantly claimed compounds are substantially embraced by the reference claims. The reference disclosed urea compounds that are useful as therapeutic agents. One of ordinary skill in the art would have been motivated to select the claimed compounds from the genus in the reference since such compounds would have been suggested by the reference as a whole because the skilled artisan would have had reasonable expectation that any of the compounds would have had the same use taught for the genus as a whole.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

(11) Response to Argument

Claim Rejections - 35 U.S.C. 112

Appellant's arguments have been fully considered but they were not deemed to be persuasive. Appellant first asserts that 'the specification provides a number of publications that have correlated the inhibition of RAF kinase with the inhibition of the growth of a variety of tumor types'. However, contrary to applicant's assertion, the state of the art references do not establish a therapeutic method for the treatment of cancerous cell growth mediated by RAF kinase generally. See e.g., Kolch (Nature 1991) provides that RAF-1 inhibitors blocked proliferation of specific oncogenes. Monia (Nat. Med. 1996) also provided a role of RAF kinase in the development of specific types of malignancies. None of the state of the art references of record expressed a single therapeutic approach for treating cancerous cell growth generally by administering a single class of compounds. Further, the state of the art is not indicative of the fact that treatment of all types of cancerous cell growth or solid cancers mediated by RAF kinase is conventional or well known. The cited references are too speculative. The references are specific with respect to limited types of cancerous growth or malignancy.

Appellant argues that 'no evidence has been presented to refute the findings or conclusions made in the publications'. However, as explained above, the findings and conclusions in the cited publications with respect to inhibition of RAF kinase and the application of such activity for specific types of cancerous growth. The instant claims, on the other hand, are

drawn to several types of cancers affecting different organs and having different methods of growth or harm to the body, and different vulnerabilities. The development of the most efficacious strategy for the treatment of cancers is based on understanding the underlying mechanisms of carcinogenesis. This includes the knowledge that the carcinogenic process is a multi-step, multi-mechanism process and that no two cancers are alike, in spite of some apparent universal characteristics, such as their inability to have growth control, to terminally differentiate, to apoptose abnormally and to have an apparent extended or immortalized life span. Since tumor promotion phase involves multiple mechanisms, there is no existence of a single therapeutic approach. The instant claims recite 'solid cancers, carcinomas, myeloid disorders or adenomas' as the cancers 'mediated by RAF kinase', however, the art does not identify a single class of compounds that can treat all these types of cancers generally.

Further, one skilled in the art of cancer therapy recognizes that there are complex interactions between individual genetic, developmental state, sex, dietary, environmental, drug, and lifestyle factors that contribute to the carcinogenic process, making it even more challenging to have a single therapeutic agent for the treatment of diverse cancers. For example, breast cancer is quite different from liver cancer and even not all breast cancers are identical to each other. Rigorously planned and executed clinical trials, incorporating measurement of appropriate biomarkers and pharmacodynamic endpoints are critical for selecting the optimal dose and schedule. A detailed understanding of the molecular mode of action of the RAF kinase inhibitors alongside the elucidation of the molecular pathology of individual cancers is required to identify tumor types and individual patients that may benefit most from treatment. It is also important to construct a pharmacologic audit trail linking molecular biomarkers and pharmacokinetic and

pharmacodynamic parameters to tumor response endpoints. There are cancers where the skill level is high and there are multiple successful chemotherapeutic treatments. In many, many cancers, however, there is no chemotherapy whatsoever available. This establishes the difficulties involved in the treatment of cancers. The various references of record have been fully considered, however, it is maintained that appellants have not provided sufficient test assays or data to support the method of treatment commensurate in scope with the claims, as of the filing date of the application.

Appellants next direct attention to specification pages 10-14 and argue that 'it would at most involve routine experimentation for one of ordinary skill in the art to treat any one of the recited cancers with a compound of the invention'. However, the specification does not enable any physician skilled in the art of medicine, to use the compound of the invention commensurate in scope with the claims. The specification broadly describes administration procedures and ranges of dosage regimen, however, it is indicated that the method of administration and/or the dose levels depend on a number of factors, which have to be evaluated by one of ordinary skill in the art. These factors include a) determining which of the claimed compounds would treat any particular claimed disease; b) synthesize the compound; c) formulate into a suitable dosage form depending the type of administration method; and d) conduct clinical trials or test the compound in an assay known to be correlated to clinical efficacy of such treatment. The specification pages 94-96 provide assays to determine the activity of the compounds, however, appellants have not asserted that it is art recognized that the assays are correlated to clinical efficacy for treatment of all types of cancerous cell growth mediated by RAF kinase. There is no working example of treatment of any disease in man or animal. The state of the clinical arts in does not provide any

chemotherapeutic agent which effective against cancers in general or those mediated by RAF kinase. There is no known chemotherapeutic drug which would target and destroy only cancer cells without adverse effects or toxicities on normal cells.

Appellants cite several case laws and argue that the enablement requirement is satisfied. This is not seen to be the case. For example, contrary to what appellants urge by citing *In re Marzocchi*,169 USPQ 367, the examiner has provided both reasoning including the nature of the invention which is directed to an unpredictable art, citation of case law as well as relevant publication to support the reason for the rejection. Appellants have not identified any state of the art references that clearly establish correlation between the assays employed in the specification and clinical efficacy for the treatment of the claimed diseases. Where the utility is unusual or difficult to treat or speculative, the examiner has authority to require evidence that tests relied on are reasonably predictive of *in vivo* efficacy by those skilled in the art. See for example *In re Ruskin* 148 USPQ 221; *Ex parte Jovanovics* 211 USPQ 907.

Appellants cite *In re Brana* and argue that 'the specification provides *in vitro* and *in vivo* assays (in pages 94-96) based on which one of ordinary skill in the art can determine the activity of each of the claimed compounds in treating various cancers. Appellant's reliance on the *Brana* decision is erroneous since the facts were different in more than one respect from the instant case. Compounds on appeal were of a much narrower scope and there were no method claims. Said compounds were similar in structure to compounds displaying *in vivo* anti-tumor activity based on art-recognized *in vivo* tests and also tested favorably in an *in vivo* test. Thus, contrary to *Brana* it is not evident that at the time of appellant's effective filing that RAF kinase inhibitors

having such a diversity of susbtituents on analogous urea compounds are well known for treating cancers urged treatable based simply on assay testing relied on herein.

Based on the fact situation of the instant application, *In re Buting*, 163 USPQ 689 (CCPA 1969) (cited in the previous office actions) is on point and more applicable to the instant claims wherein 'evidence involving a single compound and two types of cancer, was held insufficient to establish the utility of the claims directed to disparate types of cancers. The judges in that case indicated that "We are not aware of any reputable authority which would accept appellant's two clinical cases as establishing utility for treatment of cancer in humans. As was pointed out in *Brenner v. Manson*, 148 USPQ 689, a process to be patentable must produce a useful result and be of substantial utility not merely of scientific interest or for further testing. In this case further testing seems necessary".

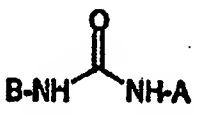
In summary, appellants have not provided any evidence of record that the instantly claimed compounds can effectively be used in the treatment of all types of cancers mediated by RAF kinase and therefore, it is maintained that one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the invention commensurate in scope with the claims.

Claim Rejections - 35 USC § 103

Appellant's arguments have been fully considered but they were not deemed to be persuasive. Appellant first argues that the method claims are not obvious over Miller et al., WO 99/32463 because the method claims recite treatment of a cancerous cell growth mediated by RAF kinase as compared to the reference which deals with treatment of p38-mediated disease

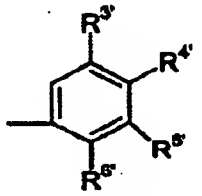
states. This is not found to be persuasive because Miller reference clearly teaches the use of diphenyl urea compounds in the treatment of various diseases (see starting in page 6) including cancer, lymphoid malignancies, etc. (see page 7) which are the same diseases intended by the instantly claimed methods, see claims 80, 81, 87 and 93. Thus, the reference teaches the administration of the same compounds to the same patient population. Applicant argues that the reference does not provide treatment of cancerous cell growth mediated by RAF kinase. This is not found to be persuasive because as explained above, Miller et al., lists therapeutic uses of the compounds in treatment various diseases including cancer. Therefore, the reference inherently teaches the instantly recited activity or mode of action of inhibition of RAF kinase activity. The instant claims recite a mode of action of RAF kinase activity, which is a property inherently possessed by the compounds of the reference. This biological property is inherently possessed by the reference compounds particularly because the compounds are used in the same therapeutic applications as recited in the instant claims. The properties possessed by the compounds, whether explicitly or inherently, can not be separated from the compounds itself.

Appellant further argues that the reference does not provide any direction to make the selections necessary to arrive at the claimed compounds. This is not found to be persuasive because the reference clearly teaches the genus encompassing the claimed species and further expressly provides compounds that are structurally analogous to the claimed compounds. The reference (WO 99/32464) teaches a generic group of compounds represented by formula I:

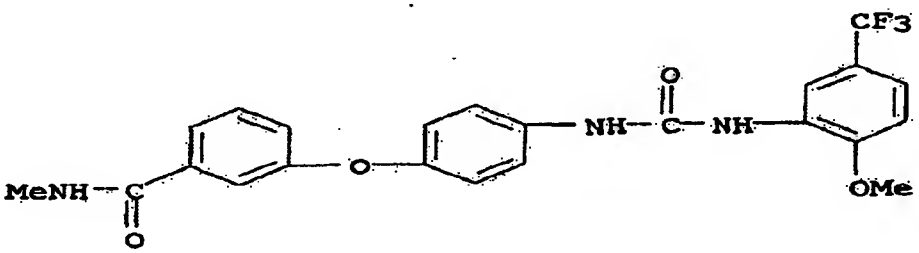


I

wherein A is

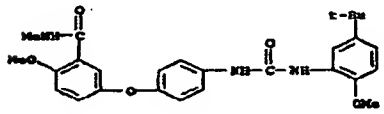


and B is phenyl substituted by –Q-Ar wherein Q is –O-, etc. and Ar is 5-10 membered aromatic structure having 0-2 ring members as heteroatoms, which aromatic structure is optionally substituted by Z_{n1} wherein Z is $-OR^7$, $-C(O)NR^7R^7$, etc. and n1 is 0-3 (see pages 7-9). The reference further teaches many species falling within the above genus, see e.g., the compound N-(5-Trifluoromethyl-2-methoxyphenyl)-N'-(4-(3-(N-methylaminocarbonyl)-phenyloxy)phenyl)urea (page 16, lines 6-7). The structural formula of the compound is depicted below for convenience:

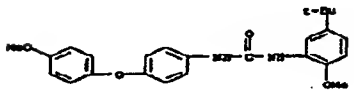


Further, the reference discloses several other compounds that are structurally analogous, see the compounds in Table 1. See for example, compound 34 in page 73, which differs from the instantly claimed compound of N-(5-tert-butyl-2-methoxyphenyl)-N'-(4-(4-methoxy-3-(N-methylcarbamoyl)phenoxy)phenyl)urea, (the first compound in claim 64) by the –C(=O)-NHMe substituent on the terminal phenyl group.

Claimed compound:



Reference compound 34:



Similarly, the second claimed compound is structurally analogous to compound 101 (page 79) of the reference. The reference clearly provides that the aromatic ring (i.e., phenyl, pyridinyl, etc.) can be substituted by Z_{n1} wherein n1 is 0 to 3 and Z definition includes $-C(O)NR^7R^7$ wherein R^7 is H, alkyl, etc. see page 9, lines 1-9. Further, the reference also provides a compound wherein the phenyl is substituted by –C(O)NHMe group, see page 16, lines 6-7 (structure depicted above). Therefore, contrary to appellant's arguments, the reference clearly teaches compounds that are structurally analogous to the instantly claimed compounds and thus, the reference provides sufficient motivation to one of ordinary skill in the art to prepare compounds having the N-methylcarbamoyl substituent.

Appellants cite *In re Baird* and argue that the genus of the reference is not sufficient to establish a *prima facie* case of obviousness for a species thereof. This is not found to be persuasive because the decision in *Baird* was based on a very large genus encompassing millions of compounds vs. a small number of claimed species, "[A] disclosure of millions of compounds does not render obvious a claim to three compounds, particularly when that disclosure indicates a preference leading away from the claimed compounds." 29 USPQ2d 1552. While the instant case involves a genus, the reference also discloses several compounds that are structurally analogous to the reference compounds, of which at least three are compared to applicant's claimed compounds (see the discussion above). Thus, the reference teaches structurally

analogous compounds which are disclosed to be useful as therapeutic agents. Therefore, motivation exists to prepare other structurally analogous compounds from the prior art disclosed genus. Such structural analogs of the reference compounds would have been obvious to one of ordinary skill in the art because the skilled chemist would have had the reasonable expectation of obtaining compounds having similar properties, i.e., pharmaceutical therapeutic agents. Reference must be considered, under 35 U.S.C. 103, not only for what it expressly teaches but also for what it fairly suggests; all disclosures of prior art, including unpreferred embodiments, must be considered in determining obviousness. *In re Burckel*, 201 USPQ 67 (CCPA 1979).

Appellants cite *In re Jones* to overcome the obviousness rejection. However, *Jones* dealt with the obviousness of a particular claimed ammonium salt based on a generic teaching of "substituted ammonium salts" with no Markush recitation for particular moiety, aminoethoxy ethanol, the salt on appeal. Secondary references applied in *Jones* were deemed not properly combinable with the generic disclosure in the primary reference since the references were not all from the same art area. Unlike the situation in *Jones*, the instantly claimed compounds are expressly taught in a single reference (Miller), which generically discloses all the elements of the instantly claimed species. Further, the instantly claimed species vary from the reference disclosed compounds only by a single ring substituent (-C(O)NHMe) which is also specifically taught for the reference compounds. Thus, the reference provides sufficient motivation for the ordinary artisan to modify the reference compounds to arrive at the instantly claimed compounds because one of ordinary skill in the art only needs to make one change to the reference disclosed compound to arrive at the instantly claimed compound.

Appellant argues that 'nothing in the reference's general disclosure suggests that compounds 34 and 101 should be modified as required to arrive at the claimed compounds'. Contrary to this argument, as explained above, the reference clearly teaches 0 to 3 substituents on the ring which include hydrogen, methoxy, methyl, chloro, phenoxy, N-methylcarbamoyl, etc., thus providing the equivalence of these groups. Thus, the reference clearly provides motivation to one of ordinary skill in adding a substituent to the expressly disclosed reference compound.

It is to be noted that rejection under 35 U.S.C. 103 is proper where the subject matter claimed "is not *identically* disclosed or described" in the prior art, and the prior art directs those skilled in the art to the compounds, without any need for picking, choosing, and combining various disclosures. See *In re Shaumann et al.*, 572 F.2d 312, 315, 316, 197 USPQ 5, 8, (CCPA 1978). Where the specific compound falls within the ambit of a "very limited number of compounds", the fact that a specific embodiment is taught to be preferred is not controlling, since all disclosures of the prior art, including unpreferred embodiments, must be considered." *In re Lamberti*, 545 F.2d 747,750, 192 USPQ 278, 280 (CCPA 1976). "The question under 35 U.S.C. 103 is not merely what the reference expressly teaches but what it would have suggested to one of ordinary skill in the art at the time the invention was made."

"Structural relationships provide the requisite motivation or suggestion to modify known compounds to obtain new compounds." See *In re Duel*, 51 F.3d at 1558, 34 USPQ2d at 1214. The closer the physical and chemical similarities between the claimed species or subgenus and any exemplary species or subgenus disclosed in the prior art, the greater the expectation that the claimed subject matter will function in an equivalent manner to the genus. See *In re Dillon*, 919

F.2d at 696, 16 USPQ2d at 1904. "An obviousness rejection based on similarity in chemical structure and function entails the motivation of one skilled in the art to make a claimed compound, in the expectation that compounds similar in structure will have similar properties." *In re Payne*, 606 F.2d 303, 313, 203 USPQ 245, 254 (CCPA 1979).

Double Patenting

The provisional rejection of claims 68, 74, 80, 81, 87 and 93 under judicially created doctrine of obviousness-type double patenting over claims 68-98 of copending application No. 10/042,203 is maintained for the reasons of record. Appellants did not present any arguments for this rejection. Appellants do not traverse this rejection but rather request it to be held in abeyance until the case is in otherwise in condition for allowance. However, the rejection must still be maintained pending the outcome of the instant appeal and/or the allowance of the copending case, which is currently under a final rejection.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

Deepak Rao
Primary Examiner
Art Unit 1624

Deepak Rao
November 19, 2004

Conferees:

1. James O. Wilson
Supervisory Patent Examiner

2. Joseph McKane
Supervisory Patent Examiner

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APPENDIX

Listing of Claims:

Claims 1-67 Canceled.

68. A compound selected from

N-(5-*tert*-butyl-2-methoxyphenyl)-*N'*-(4-(4-methoxy-3-(*N*-methylcarbamoyl)phenoxy)phenyl)urea,

N-(2-methoxy-5-(trifluoromethyl)phenyl)-*N'*-(4-(2-(*N*-methylcarbamoyl)-4-pyridyloxy)phenyl)urea,

N-(4-chloro-3-(trifluoromethyl)phenyl)-*N'*-(4-(2-carbamoyl-4-pyridyloxy)phenyl)urea,

N-(4-chloro-3-(trifluoromethyl)phenyl)-*N'*-(4-(2-N-methylcarbamoyl)-4-pyridyloxy)phenyl)urea; and

N-(2-methoxy-4-chloro-5-(trifluoromethyl)phenyl)-*N'*-(3-(2-N-methylcarbamoyl)-4-pyridyloxy)phenyl)urea,

or a mixture thereof.

Claims 69-73 Canceled.

74. A method for the treatment of a cancerous cell growth mediated by RAF kinase comprising administering one or more compounds which are:

N-(5-*tert*-butyl-2-methoxyphenyl)-*N'*-(4-(4-methoxy-3-(*N*-methylcarbamoyl)phenoxy)phenyl)urea,

N-(2-methoxy-5-(trifluoromethyl)phenyl)-*N'*-(4-(2-(*N*-methylcarbamoyl)-4-pyridyloxy)phenyl)urea,

N-(4-chloro-3-(trifluoromethyl)phenyl)-*N'*-(4-(2-carbamoyl-4-pyridyloxy)phenyl)urea,

N-(4-chloro-3-(trifluoromethyl)phenyl)-*N'*-(4-(2-N-methylcarbamoyl)-4-pyridyloxy)phenyl)urea; or

N-(2-methoxy-4-chloro-5-(trifluoromethyl)phenyl)-*N'*-(3-(2-N-methylcarbamoyl)-4-pyridyloxy)phenyl)urea.

Claims 75-79 Canceled.

80. A method as in claim 74 for the treatment of solid cancers.

81. A method as in claim 74 for the treatment of carcinoma, myeloid disorders or adenomas.

Claims 82-86 Canceled.

87. A method as in claim 74 for the treatment of carcinoma of the lung, pancreas, thyroid, bladder or colon.

Claims 88-92 Canceled.

93. A method as in claim 74 for the treatment of myeloid leukemia or villous colon adenomas.

Claims 94-98 Canceled.